09/056072

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/056,072	04/07/98	BAZIN	H 61750221

HM11/0707

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EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	4

DATE MAILED: 07/07/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 30-43 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 30-43 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ NOTICE TO COMPLY SEQUENCE RULES

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-410-238/4

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Technology Center 1600.

2. Applicant's amendments, filed 4/7/98 (Paper Nos. 2/3), is acknowledged.
Claims 1-29 have been canceled.
Claims 30-43 have been added.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825, however, this application fails to comply with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

Applicant is required to fulfill these requirements by defining the SEQ ID NOS in both the specification and claims.

The following procedure is to be used for cases that contain the same sequence disclosure as the parent. The applicant need not submit a new computer readable from of the Sequence Listing in this rule 60 continuation. However, (1) the specification must contain a paper copy of the Sequence Listing, (2) applicant must request in writing that the CRF in the parent case be used to prepare a file for the offspring and (3) applicant must submit a statement that the paper copy of the Sequence Listing in the offspring is identical to the computer readable form submitted in the parent case.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

5. The Specification is objected to because there appears to be no Summary of the Invention disclosed in the instant application. Applicant is reminded that no new matter should be added to the specification.

6. The disclosure is objected to because of the following informalities:

Page 23, Example 2 of the specification refers to Appendix 1, however the information indicated in Appendix 1 should be incorporated into body of the specification as a Table or added as a Figure. An Appendix is not proper.

The specification is replete of trademarks. The use of trademarks such as "OKT3", "KETALAR", "PRAZINE", etc. are noted in this application. They should be capitalized and/or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

The application is required to be reviewed and all spelling and like errors corrected. Appropriate corrections are required.

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The specification is objected to and claims 30-43 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

It unclear if a cell line which produces an antibody having the exact structural and chemical identity of the HB 11423 hybridoma which produces the LO-CD2a antibody is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event. Deposit of the appropriate hybridoma under the Budapest Treaty with appropriate assurances would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Alternatively, applicant may satisfy the deposit requirement for LO-CD2a antibody itself, if the amino acid sequence of the entire LO-CD2a antibody is disclosed and recited in the claims. However, the sequence of the LO-CD2a antibody does not satisfy the deposit of the HB 11423 hybridoma.

Affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

9. Claims 34 and 42 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34 and 42 are indefinite in the recitation of "chimeric" because the metes and bounds is unclear. For example, chimeric can refer simply to variable (e.g murine) region - constant region (e.g. human) constructs, while humanized would refer to CDR-grafted antibodies. Chimeric antibodies can be a broad term that encompass any number of recombinant forms of antibodies. To clearly define the metes and bounds of said chimeric antibody, applicant is invited to amend the claims to recite that chimeric antibodies refer to variable (e.g murine) region - constant region (e.g. human) constructs. This would distinguish said "chimeric" antibodies from other recombinant forms as well as the other recited form of "humanized" antibodies, which are also chimeric, but refer to CDR-grafted antibodies.

The amendments must be supported by the specification so as not to add any new matter.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made. Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

13. Claims 30-32, 35-40 and 43 are rejected under 35 U.S.C. § 102(b) as being anticipated by Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) Xia et al. teach the LO-CD2a-specificity, including hybridomas and methods of making said antibodies and hybridomas of the instant invention (see entire document and page 312 for example). Although the reference is silent about a pharmaceutically acceptable carrier per se, the storage and use of the LO-CD2a antibody in pharmaceutically acceptable carriers such as PBS was well known, practiced and immediately envisaged at the time the invention was made in the art. In addition, the intended use or amount to elicit alloantigen specific hyporesponsiveness would have been met by the reference as such claimed amounts encompass a broad range as the amount of antibody to elicit said immunosuppression would depend on the nature of the system being analyzed or tested.

14. Claims 30-43 are rejected under 35 U.S.C. § 103 as being unpatentable over Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) in view of Queen et al. (U.S. Patent No. 5,530,101) or Newman et al. (U.S. Patent No. 5,658,570) and in further view of Guckel et al. (J. Exp. Med., 1991) OR Bromberg et al. (Transplant., 1991) OR Hafler et al. (J. Immunol., 1988) OR Chavin et al. (Transplant., 1992) OR Faustman (U.S. Patent No. 5,283,058). The instant claims are drawn to antibodies that bind the LO-CD2 specificity, including chimeric and humanized antibodies, as well as cell that produced said antibodies and methods of making said antibody. .

Xia et al. provides a number of phenotypic and functional characteristics that are associated with the LO-CD2a specificity (see entire document). Also, Xia et al. distinguishes the LO-CD2a specificity from other CD2-specific antibodies and clearly discloses that this specificity binds a different epitope from other CD2-specific antibodies (for example, see page 320, paragraphs 1-3). It would have been expected at the time the invention was made that different antibodies would recognize the same conformational epitope, which is the LO-CD2 epitope in the instant case. The prior art clearly set forth numerous features that characterize and enable one of skill in the art at the time the invention was made to make an antibody that binds to the same LO-CD2 epitope specificity as claimed. Xia et al. Differs from the instant claims by not disclosing chimeric or humanized antibodies per se.

Queen et al. teaches the art-known procedures at the time the invention was made to produce chimeric antibodies starting from hybridoma and antibody producing cells.

Similarly, Newman et al. Teach the generation of recombinant antibodies including CD2-specific antibodies for various diagnostic and therapeutic uses. While it is noted that Newman et al. Teaches the use of Old World Monkey portions in the derivation of recombinant antibodies, this reference clearly recognizes the derivation of chimeric and humanized antibodies at the time the invention was made and that CD2 was a desired specificity at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have generated chimeric or humanized antibodies in order to reduce immunogenicity while retaining high binding affinity for diagnostic and therapeutic purposes as well as the appropriate vectors, host cells, etc. to accomplish the engineering of chimeric and humanized antibodies (see entire documents). Therefore, Queen et al. Or Newman et al. teach that immunoglobulin gene structure and organization were well understood in the art at the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs comprising expression vectors containing DNAs encoding immunoglobulin variable regions. Queen et al. And Newman et al. differ from the claimed invention by not teaching the LO-CD2a specificity per se, the ordinary artisan would have been motivated to apply the teachings of Queen et al. Or Newman et al. to enable the isolation and construction of chimeric and humanized antibodies that bind the LO-CD2a specificity.

In addition to the LO-CD2a specificity, the instant claims also encompass antibodies that elicit alloantigen specific unresponsiveness. Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman all teach the art-known potent inhibition of immune responses by blocking or modulating T cell surface receptors such as CD2 that are important in adhesion receptor-signaling (see entire documents particularly the Introductions and Discussions).

Guckel et al. teach the ability of rat anti-CD2 antibodies to induce T cell unresponsiveness in vivo in mice (see entire document). CD2-specific antibody inhibition of transplants and autoimmunity is taught (page 965, column 2, paragraph 2).

Bromberg et al. teach that anti-CD2 antibodies alter cell-mediated immunity in vivo by altering the array of cell surface receptors and subsequent responses to antigenic challenge (see entire document). Bromberg et al. also teach the potent immunosuppressive properties of anti-CD2 antibodies for murine allografts and xenografts as well as for primate skin and renal allografts (page 224, column 1, paragraph 1).

Hafler et al. teach that anti-CD2 antibodies inhibit T cell responses in human patients with progressive multiple sclerosis (see entire document). Hafler et al. also teach that T cell-specific antibodies have been used successfully as immunosuppressive reagents in transplant rejections and autoimmune diseases (see Introduction).

Chavin et al. teaches the efficacy of treating allografts and xenografts in vivo with CD2-specific antibodies (see entire document, particularly the Introduction and Discussion). Prolonged allograft survival correlated with suppression of both CTL and NK activity (page 290, column 1, paragraph 3 and Table 2). Here, Chavin et al. concludes by stating that the ability of anti-CD2 antibodies to suppress lymphocyte precursors and T and non-T cell responses supports its use for induction therapy in transplantation.

Faustman teaches methods of inhibiting the rejection of allografts and xenografts with T cell-specific antibodies and antibody fragments including the CD2-specificity (see entire document, including column 5, paragraph 1). Such methods of inhibiting rejection include modifying, eliminating and masking an antigen on the surface of a cell (see entire document, including Abstract).

It would have prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the LO-CD2-specific antibodies to characterize the CD2 specificity and to target said specificity for various biological, diagnostic and therapeutic modalities. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 30-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-26 of copending application Serial No. 08/477,989. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to same or similar LO-CD2-specific antibodies, including chimeric and humanized antibodies.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 30-43 are directed to an invention not patentably distinct from claims 11-26 of copending application Serial No. 08/477,989. Specifically, the conflicting claims are patentably distinct from each other because both applications are drawn to same or similar chimeric and humanized LO-CD2-specific antibodies, including chimeric and humanized antibodies.

Commonly assigned 08/477,989, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, Ph.D.
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Technology Center 1600
July 6, 1998